REMARKS

Reconsideration is requested.

Claims 15-17 and 22 have been canceled, without prejudice.

Claims 1-14, 18-21 and 23-35 are pending. Claims 26-35 have been added. Support for the additional claims and amendments can be found throughout the specification and originally-filed claims. Specifically, support for the amendments can be found, for example, at page 5, lines 4-18 and page 6, lines 4-8 as well as originally-filed claim 2. Further support may be found, for example, at page 8, line 28. New claims 26-28 include a definition of the fatty acid based, for example, on the experimental section of the application. The fatty acids defined by claim 27 are all capable of inducing apoptosis as detected by a DNA ladder in Figure 3, right side and the fatty acids in claim 28 results in a high biological activity of the alpha-lactalbumin complex as described in the table in Figure 3. No new matter has been added.

The Section 112, second paragraph, rejection of claims 1-14 and 18-25 is believed to be obviated by the above amendments. Claim 1 has been revised and new claim 29 added to at least obviate the Examiner's comments relating to the objection of claims 2 and 5. Withdrawal of the rejection is requested.

To the extent not obviated by the above amendments, the Section 112, first paragraph "written description", rejection of claims 1-14 and 18-19 is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments.

The applicants believe the pending claims are adequately described by the present specification. The applicants believe that one of ordinary skill in the art will

appreciate that the applicants were in possession of the claimed invention at the time the application was filed.

Specifically, the fragments of the claims are described, for example, on page 6, lines 4-7 of the specification. The Examiner will appreciate that SEQ ID NOs: 1 and 2 contain 123 amino acids. Fragments of the claims therefore require more than 81% of SEQ ID NO:1 or SEQ ID NO:2. As described below, the applicants believe that one of ordinary skill in the art will appreciate from the generally advanced level of skill in the art, as well as the present disclosure, that the applicants had possession of the claimed fragments at the time the application was filed in that fragment of at least 100 amino acids containing SEQ ID NO:1 or SEQ ID NO:2 which retained the required function could be reasonably identified from the alignments available from the art in view of the present disclosure.

Similarly, variants of the claims are described in the present specification at, for example, page 5, lines 4-18. As described below, the applicants believe that one of ordinary skill in the art will appreciate from the generally advanced level of skill in the art, as well as the present disclosure, that the applicants had possession of the claimed variants at the time the application was filed in that variants containing at least 95% sequence identity to SEQ ID NO:1 or SEQ ID NO:2 which retained the required function could be reasonably identified from the alignments available from the art in view of the present disclosure.

Specifically, the ordinarily skilled person will appreciate that alpha lactalbumin sequences from multiple species are highly homologous.

An alignment of alpha-lactalbumin from multiple species is available, for example, in Watanabe, M et al ((2000) J. Vet. Med. Sci. 62(11):1217-1219) (filed with Information Disclosure Statement filed December 20, 2006; return of an initialed copy of the PTO 1449 Form listing the same, pursuant to MPEP § 609, is requested). A person of ordinary skill in the art will appreciate from this generally advanced level of skill in the art and the present specification that the applicants were in possession of the claimed invention at the time the application was filed. One of ordinary skill will appreciate, for example, that non-conserved residues are possibly mutated, positions marked with a "." Or ":" are indicative of positions which tolerate at least conservative modifications. One of ordinary skill will further appreciate that positions marked with an asterisk are conserve residues which are preferably not modified unless otherwise specified, such as is further explained below. Accordingly, based on an alignment available in the art at the time the present application was filed, or alpha-lactalbumin from different species, a person or ordinary skill is able to appreciate that that applicants adequately describe the claimed invention by relying, for example, on this generally advanced level of skill in the art. One of ordinary skill will appreciate that the present specification describes suitable variants comprising, for example, one or more amino acid substitutions without interfering with the function of the protein. In the particular instance wherein mutations in specific regions are desired, such as for disruption of the Ca^{2+} binding region, mutations of conserved residues will be recognized as being preferred.

The ordinarily skilled person will appreciate that the present application describes a variety of variants of human or bovine alpha-lactalbumin that may be used according to the present invention. Based on knowledge from Svensson (2000) (or record), such

variants are readily purified from *E. coli*. The art therefore provides methods for one of ordinary skill in make the variants and fragments.

The applicants further note, with regard to the objected-to recitation of "unsaturated cis fatty acid", the presently claimed cofactor is an unsaturated fatty acid which has a configuration similar to C18:1:9 or C18:1:11 with the proviso that the cofactor is not C18:1:9 cis (oleic acid). The application describes the surprising finding that unsaturated fatty acids different from oleic acid can participate in forming a biologically active complex. The description describes, for example, the activity of several C16-C18 unsaturated fatty acids. The application and generally advanced level of skill in the art describe methods of evaluating further suitable cofactors capable of stabilizing the complex in a biologically active form. The claims are submitted to be supported by an adequate written description.

Withdrawal of the Section 112, first paragraph "written description", rejection is requested.

The Section 102 rejection of claims 1-6, 9, 13, 14 and 19 over Swenson (PNAS (April 11, 2000), Vol. 97, No. 8, pp 4221-4226), and the Section 102 rejection of claims 1-5, 14, 18 and 19 over Hakansson (Molecular Biology, 2000, 35(3), pp 589-600) are believed to be obviated by the above amendments, which emphasize that the cofactor of the claims is not oleic acid (i.e., C18:1:9 cis) where the alpha-lactalbumin components are as described in the above pending claim 1.

Specifically, Swenson et al is understood to describe human alpha-lactalbumin in complex with oleic acid (C18:1:9cis). The cited art is understood to further describe that only oleic acid is capable of stabilizing the active complex. While the cited art uses the

general term C18:1 fatty acid, the ordinarily skilled artisan will appreciate from, for example, page 4222, second column, line 17, of the cited art, that only oleic acid (C:18:1:9cis) has been used and consequently the cited art is believed to only literally describe the functionality of oleic acid as cofactor.

The claims are patentable over the cited Swenson document and withdrawal of the Section 102 rejection based on the same is requested.

The cited Hakansson document is understood to describe HAMLET, and as seen on page 598, second column, line 8, the alpha-lactalbumin complex is prepared using oleic acid. Although the general term C18:1 fatty acid, as D2, is used in the text, one of ordinary skill will appreciate that the only functional cofactor disclosed is oleic acid (C:18:1:9cis). Table 2 of the cited art is understood to show the bactericidal activity for different folding variants of alpha-lactalbumin and different fatty acids. As described in the paragraph spanning page 593, second column and page 584, first column, of the cited art, no bactericidal activity was detected testing C18:1, C16:0 and C14:0 alone, but only when converted alpha –lactalbumin was tested.

The claims are patentable over the cited Hakansson document and withdrawal of the Section 102 rejection based on the same is requested.

To the extent not obviated by the above amendments, the Section 103 rejection of claims 1 and 6-8 over Swensson and Permyakov (Protein Engineering, Vol. 14, No. 10, pp 785-789, 2001), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the above and the following comments.

Specifically, as described above, the cited art is believed to teach that only association of alpha-lactalbumin with oleic acid leads to formation of a biological active

complex. There was no motivation or suggestion in the cited art have believed otherwise and the presently claimed invention is believed to have been contrary to the teachings of the cited art. Permyakov et al is understood to relate to Ca^{2+} affinity of alpha-lactalbumin mutants D87A and D87N. Combining Swenson et al with Permyakov et al however would not have provided any reasonable expectation of successfully making the presently claimed invention. It was contrary to the cited Swenson to have predicted the claimed invention could have been made which requires, for example, a cofactor other than oleic acid.

Withdrawal of the Section 103 rejection is requested.

The objection to claims 1, 10 and 20-25 are obviated by the above amendments. Withdrawal of the objections is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested. The Examiner is requested to contact the undersigned in the event anything further is required.

Respectfully submitted,

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